4,4'-Methylenebis(N,N-dimethyl)-benzenamine

CAS No. 101-61-1

Reasonably anticipated to be a human carcinogen

First listed in the Third Annual Report on Carcinogens (1983)

Also known as Michler's base or or p,p'-tetramethyldiamino-diphenylmethane

Carcinogenicity

4,4'-Methylenebis(*N*,*N*-dimethyl)benzenamine is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in experimental animals.

Cancer Studies in Experimental Animals

Oral exposure to 4,4'-methylenebis(*N*,*N*-dimethyl)benzenamine caused tumors in two rodent species and at two different tissue sites. Dietary administration of 4,4'-methylenebis(*N*,*N*-dimethyl) benzenamine caused cancer of the thyroid gland (follicular-cell carcinoma) in rats of both sexes and increased the combined incidence of benign and malignant liver tumors (hepatocellular adenoma and carcinoma) in female mice (NCI 1979).

Cancer Studies in Humans

No epidemiological studies were identified that evaluated the relationship between human cancer and exposure specifically to 4,4'-methylenebis(*N*,*N*-dimethyl)benzenamine.

Properties

4,4'-Methylenebis(*N*,*N*-dimethyl)benzenamine is a bicyclic aromatic amine that exists at room temperature as yellowish glistening leaflets or plates or as tan crystals with a faint odor (NCI 1979, Akron 2009, HSDB 2009). Commonly referred to as Michler's base, it is the reduced form of Michler's ketone, which is listed in the Report on Carcinogens as *reasonably anticipated to be a human carcinogen*. 4,4'-Methylenebis(*N*,*N*-dimethyl)benzenamine is practically insoluble in water, slightly soluble in cold alcohol, and soluble in hot alcohol, benzene, diethyl ether, carbon disulfide, and acids (ChemIDplus 2009, HSDB 2009). It is stable under normal temperatures and pressures (Akron 2009). Physical and chemical properties of 4,4'-methylenebis(*N*,*N*-dimethyl)benzenamine are listed in the following table.

| Property | Information |
|-------------------------------|---------------------------------|
| Molecular weight | 254.4ª |
| Density | 1.14 g/cm³ at 20°C ^b |
| Melting point | 90°C to 91°C ^a |
| Boiling point | 390°Cª |
| Log K _{ow} | 4.37° |
| Water solubility | 4.14 mg/L at 25°C ^c |
| Vapor pressure | 1.75 × 10⁻⁵ mm Hg at 25°C° |
| Vapor density relative to air | 8.77 ^b |

Sources: aHSDB 2009, bAkron 2009, ChemIDplus 2009.

Use

4,4'-Methylenebis(*N*,*N*-dimethyl)benzenamine is used as an intermediate in the manufacture of at least six dyes and one pigment (including methylene red and C.I. basic yellow 2, basic orange 14, solvent orange 15, and solvent yellow 34). Its hydrochloride salt is used as an analytical reagent for the determination of lead (IARC 1982).

Production

Commercial production of 4,4'-methylenebis(*N*,*N*-dimethyl)benzenamine in the United States began in the early 1920s (IARC 1982). U.S. production was approximately 1.8 million pounds in 1974, decreasing to 1.0 million pounds in 1977. In 2009, 4,4'-methylenebis(*N*,*N*-dimethyl)benzenamine was produced by one manufacturer each in China, Europe, and India (SRI 2009) and was available from 16 suppliers, including 10 U.S. suppliers (ChemSources 2009). Reports filed under the U.S. Environmental Protection Agency's Toxic Substances Control Act Inventory Update Rule indicated that U.S. production plus imports of 4,4'-methylenebis(*N*,*N*-dimethyl)benzenamine totaled 500,000 lb to 1 million pounds in 1986 and 10,000 to 500,000 lb in 1990 (EPA 2004); no inventory update reports for 4,4'-methylenebis(*N*,*N*-dimethyl)benzenamine were filed in 1994, 1998, or 2002.

Exposure

The routes of potential human exposure to 4,4'-methylenebis(*N*,*N*-dimethyl)benzenamine are inhalation, ingestion, and dermal contact (NJDHSS 2009). EPA's Toxics Release Inventory reported environmental releases of 8,400 lb in 1988, 10 lb in 1995, and 1 lb in 1996; no more recent releases have been reported (TRI 2009). Although the compound is relatively nonvolatile, workers may be exposed via inhalation of dust. The potential for exposure is greatest among workers in the dye and chemical manufacturing industries (NCI 1979). The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 4,140 workers potentially were exposed to 4,4'-methylenebis(*N*,*N*-dimethyl)benzenamine (NIOSH 1990).

Regulations

Environmental Protection Agency (EPA)

Emergency Planning and Community Right-To-Know Act Toxics Release Inventory: Listed substance subject to reporting requirements.

References

Akron. 2009. The Chemical Database. The Department of Chemistry at the University of Akron. http://ull. chemistry.uakron.edu/erd and search on CAS number. Last accessed: 8/11/09.

ChemlDplus. 2009. ChemlDplus Advanced. National Library of Medicine. http://chem.sis.nlm.nih.gov/chemidplus/chemidheavy.jsp and select Registry Number and search on CAS number. Last accessed: 8/11/09.

ChemSources. 2009. *Chem Sources - Chemical Search*. Chemical Sources International. http://www.chemsources.com/chemonline.html and search on tetramethyldiaminodiphenylmethane. Last accessed: 8/11/09

EPA. 2004. Non-confidential IUR Production Volume Information. U.S. Environmental Protection Agency. http://www.epa.gov/oppt/iur/tools/data/2002-vol.html and search on CAS number. Last accessed: 4/21/05.

HSDB. 2009. Hazardous Substances Data Bank. National Library of Medicine. http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB and search on CAS number. Last accessed: 8/11/09.

IARC. 1982. 4,4'-Methylenebis(N,N-dimethyl)benzenamine. In *Some Aromatic Amines, Anthraquinones* and *Nitroso Compounds and Inorganic Fluorides Used in Drinking Water and Dental Preparations,* vol. 27. Lyon, France: International Agency for Research on Cancer. pp. 119-126.

NCI. 1979. *Bioassay of 4,4'-Methylenebis-*(N,N-*dimethyl)benzenamine for Possible Carcinogenicity.* Technical Report Series no. 186. DHEW (NIH) Publication No. 79-1742. Bethesda, MD: National Institutes of Health.

NIOSH. 1990. National Occupational Exposure Survey (1981-83). National Institute for Occupational Safety and Health. Last updated: 1990. http://www.cdc.gov/noes/noes1/m3405sic.html. Last accessed: 1/24/05.

Report on Carcinogens, Twelfth Edition (2011)

NJDHSS. 2009. Hazardous Substance Fact Sheet: 4,4'-Methylenebis(N,N-Dimethyl)Benzenamine. New Jersey Department of Health & Senior Services. http://nj.gov/health/eoh/rtkweb/documents/fs/1252.pdf. SRI. 2009. Directory of Chemical Producers. Menlo Park, CA: SRI Consulting. Database edition. Last accessed: 8/11/109

TRI. 2009. TRI Explorer Chemical Report. U.S. Environmental Protection Agency. http://www.epa.gov/triexplorer and select 4,4'-Methylenebis(N,N-Dimethyl)benzenamine.